An Overview of Regulatory and Trust Issues for the Integrated Clinical Environment

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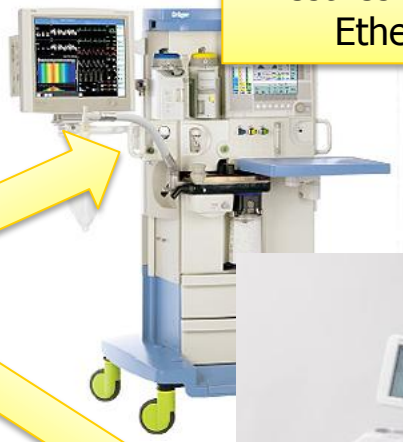
Network Enabled Devices…

Many modern medical devices are network-enabled…

RxStation / Ethernet

Ethernet / 802.11b



Anesthesia Machine Ethernet

RS-232 to Ethernet Adapter

Portable Monitor 802.11b

ECG Cart Ethernet

How is this connectivity being leveraged in emerging commercial products?

Cerner SmartRoom

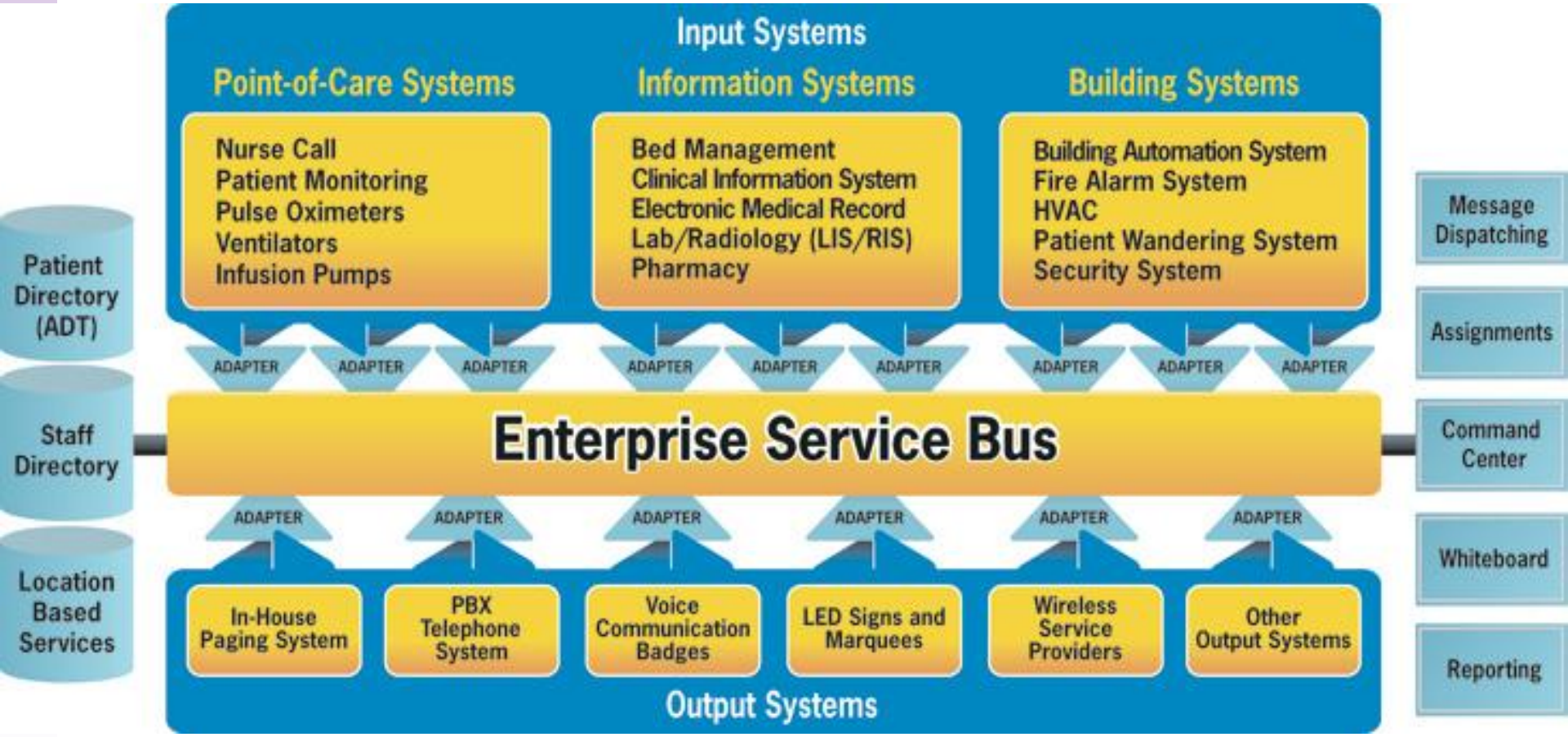
Integrated displays with views customized for caregiver

Networked Devices

Enterprise Service Bus

Electronic Patient Medical Record

Philips / Emergin



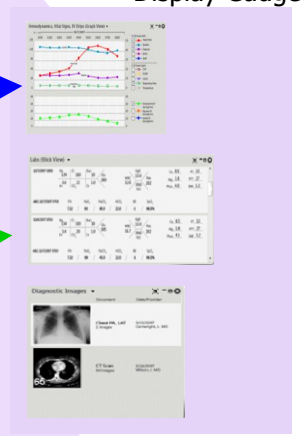
Emergin System ESB product graphic

Emerging Commercial Systems

Medical Device Data Systems (MDDS) -- Data only flows from producers to consumers; data must be faithfully re-presented

Devices

Data Consumers



EMR Databases

Current FDA regulations do not allow any automated control of devices/settings or significant reformatting of data.

From *Integration* to *Systems*

Looking ahead…

- Delivering modern medical care involves complex cyber-physical systems…
  - many medical devices, electronic medical records, clinicians/care-givers …all working together to achieve a goal

- Although most modern medical devices have some form of connectivity, they are not integrated so that they can work together as a system
  - devices are "unaware of their context", e.g., details of patient parameters, history, current procedures they may impact/distort readings
  - data from multiple devices is not combined to produce more meaningful information to clinicians
  - actions of multiple devices cannot be automatically coordinated to achieve greater safety and efficiency

How might health care delivery benefit if devices and EHR databases could function as components of automated systems?

Safety Interlocks

Fully leverage device data streams and the ability to *control* devices

Devices

***Moving forward**: aggregating data streams to solve **systems problems** by making devices context aware.*

Data Consumers

Display Gadgets

O_2 Conc. Data

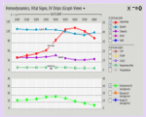
Laser Activation Data

Laser Disable Command

Disable laser if inspired O_2 is > 25%.

Safety Interlock Logic

Alarm Info



Surgical Team

Tracheal tube fire hazard -- caused by failure to reduce O_2 concentration during tracheal laser surgery

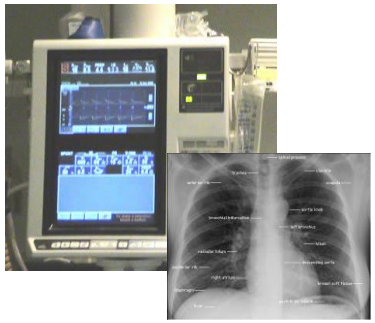
Proposed and published by Sem Lampotang, PhD, Univ. of Florida -- not commercially available. Device coordination systems can provide a solution.

From Dr. Julian Goldman -- MDPnP.

Problematic Clinical Workflows

Example Use-Case: X-Ray / Ventilator Interaction

- Constant movement of a patient on ventilator makes it difficult to acquire x-ray image.
- Clinicians often manually disable ventilators -- sometimes with very bad consequences



A 32-year-old woman had a laparoscopic cholecystectomy [gall bladder removal] performed under general anesthesia. At the surgeons request, a plane film x-ray was shot during a cholangiogram [bile duct image]. The anesthesiologist stopped the ventilator for the film. The x-ray technician was unable to remove the film because of its position beneath the table. The anesthesiologist attempted to help her, but found it difficult because the gears on the table had jammed. Finally, the x-ray was removed, and the surgical procedure recommenced. At some point, the anesthesiologist glanced at the EKG and noticed severe bradycardia. He realized he had never restarted the ventilator. ***This patient ultimately expired****.*

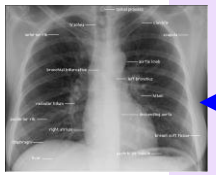
2005 Anesthesia Patient Safety Foundation Newsletter

Device Coordination

Fully leverage device data streams and the ability to *control* devices

Devices

***Moving forward**: live detection of patterns in monitoring data, automation of sequences of tasks in a clinical workflow*

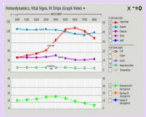


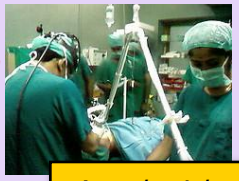
X-Ray Activation

Pause ventilator and activate x-ray when appropriate waveform point is signaled

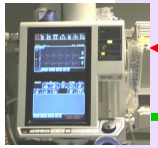
Device Task controller

Confirmation Control





Anesthesiologist



Ventilator Pause Command

Breathing Pattern Data

Single appropriate waveform point

Breathing Waveform Monitor

From Dr. Julian Goldman -- MDPnP.

Closed Loop Control

Example Use-Case: PCA Monitoring

- Patients are commonly given patient-controlled analgesics after surgery
  - …better outcomes than nurse administered opioids
- Administers analgesics such as morphine, fentanyl, and hydromorphone
  - constant basal rate of infusion
  - bolus does delivered when patient pushes button

PCA Pump

Opioid Side-Effects -- Respiratory Depression

- decreased respiratory rate, decreased oxygen saturation, increased end tidal carbon dioxide
- detect by monitoring
  - heart rate, respiration rate, blood pressure
  - pulse oximeter (oxygen saturation)
  - capnography (CO_2 exhalation)

PCA Hazards

- operator error (wrong drug, wrong dosage)
- PCA by proxy
  - e.g., relative pushes button for patient
- monitoring device alarms tends to lag time of overdose

Closed Loop Control

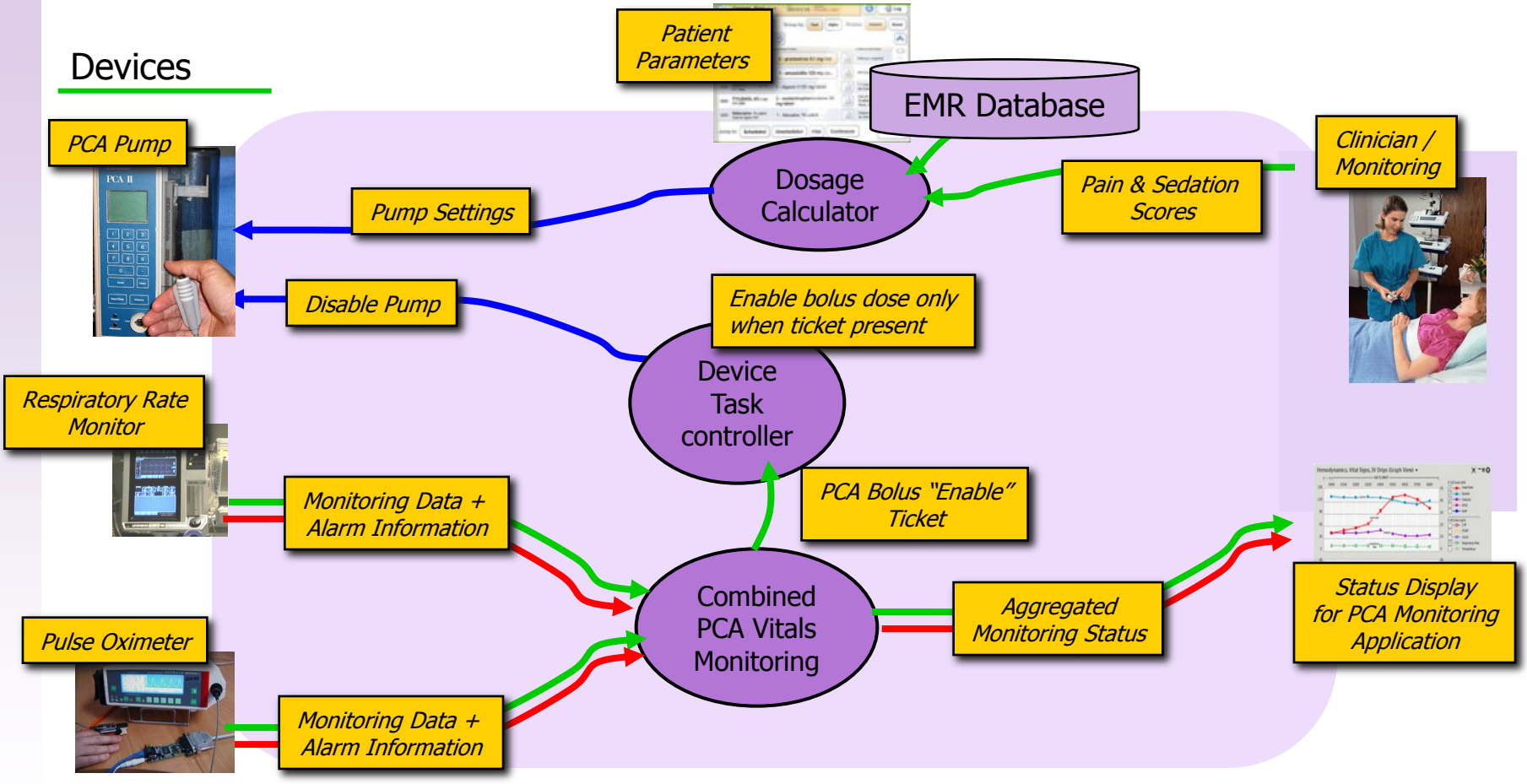
Example Use-Case: PCA Monitoring

- Patients are commonly given patient-controlled analgesics after surgery
- There have been occurrences of patients overdosing

A 49-year old woman underwent an uneventful operation (total abdominal hysterectomy and bilateral salpingo-oophorectomy). Postoperatively, the patient complained of severe pain and received intravenous morphine sulfate in small increments. She began receiving a continuous infusion of morphine via a patient controlled analgesia (PCA) pump. A few hours after leaving the PACU [post anethesia care unit] and arriving on the flow, she was found pale with shallow breathing, a faint pulse, and pinpoint pupils. The nursing staff called a "code", and the patient was resuscitated and transferred to the intensive care unit on a respirator. Based on family wishes, life support was withdrawn and the patient died. Review of the case implicated a PCA overdose. Delayed detection of respiratory compromise in patients undergoing PCA therapy is not uncommon because monitoring of respiratory status has been confounded by excessive nuisance alarms.

Closed Loop Control

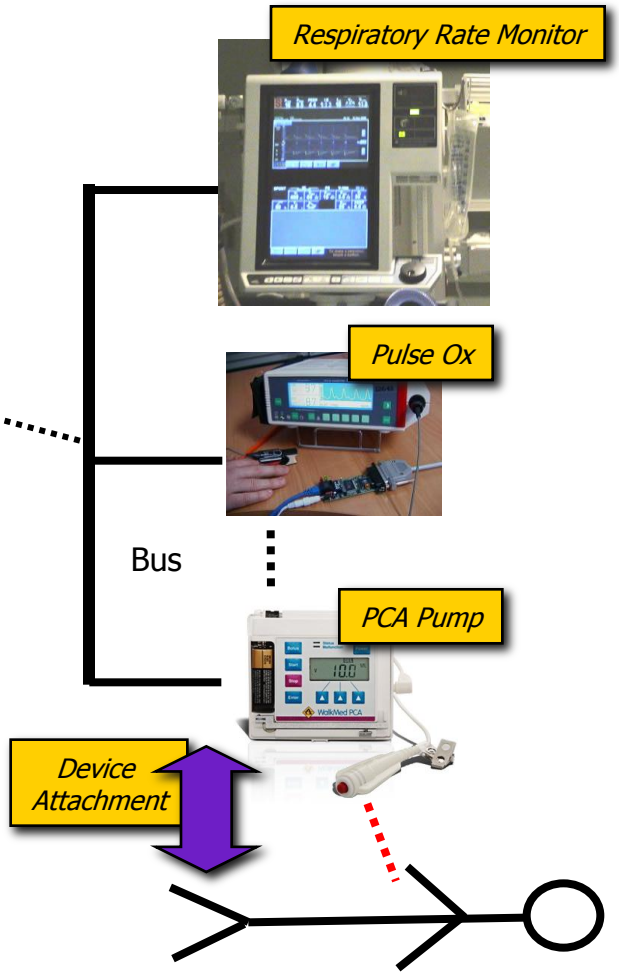
Fully leverage device data streams and the ability to *control* devices



Vision: Integrated Clinical Environment (ICE)

Develop a bus-based app for implementing a safety interlock by coordinating monitoring of vitals with pump control…

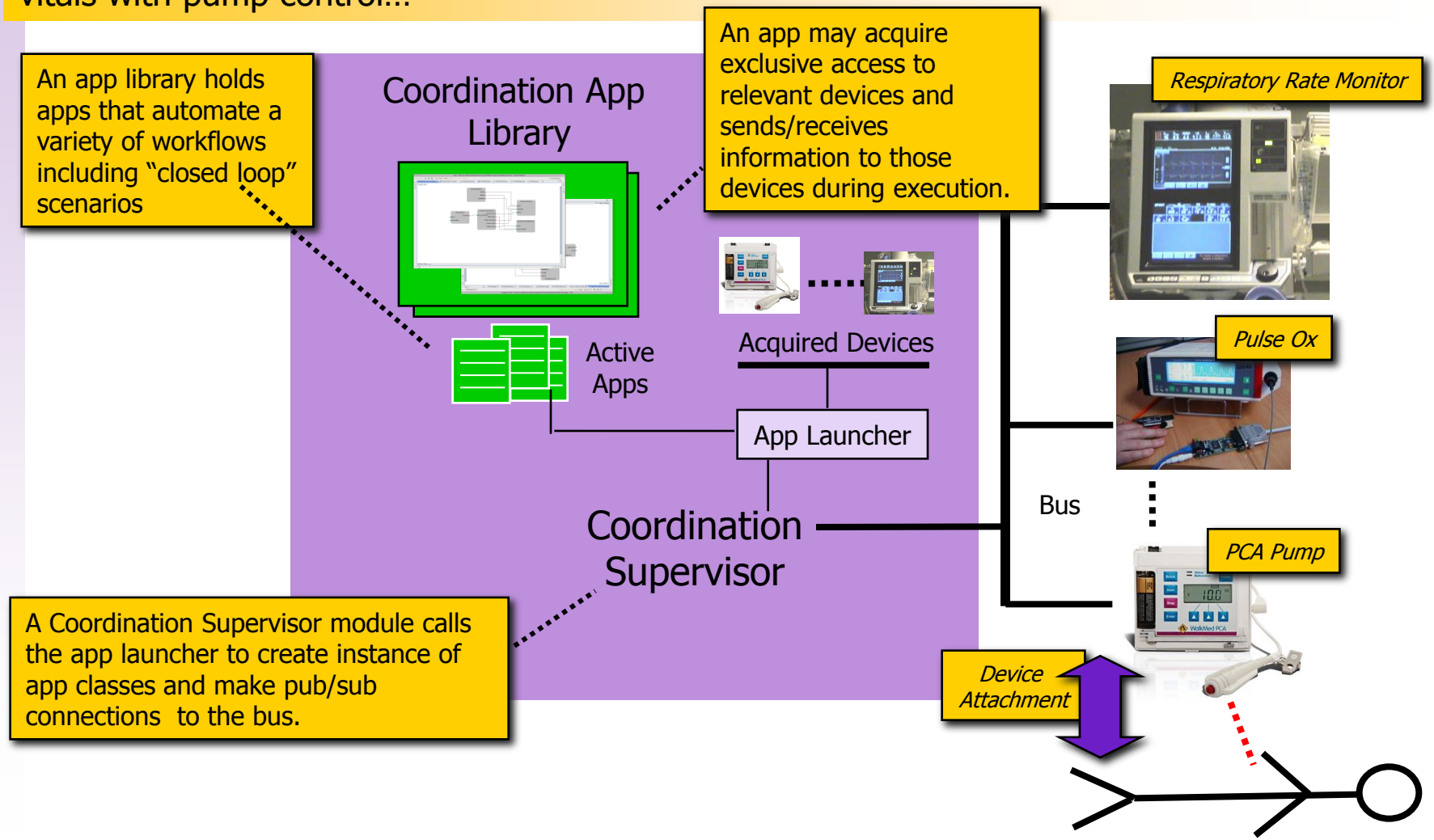
Pulse ox, respiratory rate monitor, infusion pump with hand-held control are connected to the patient.



ASTM F2761-09 *Essential safety requirements comprising the patient-centric integrated clinical environment (ICE) --- Part 1: General requirements and conceptual model*

Functional View

Develop a bus-based app for implementing a safety interlock by coordinating monitoring of vitals with pump control…



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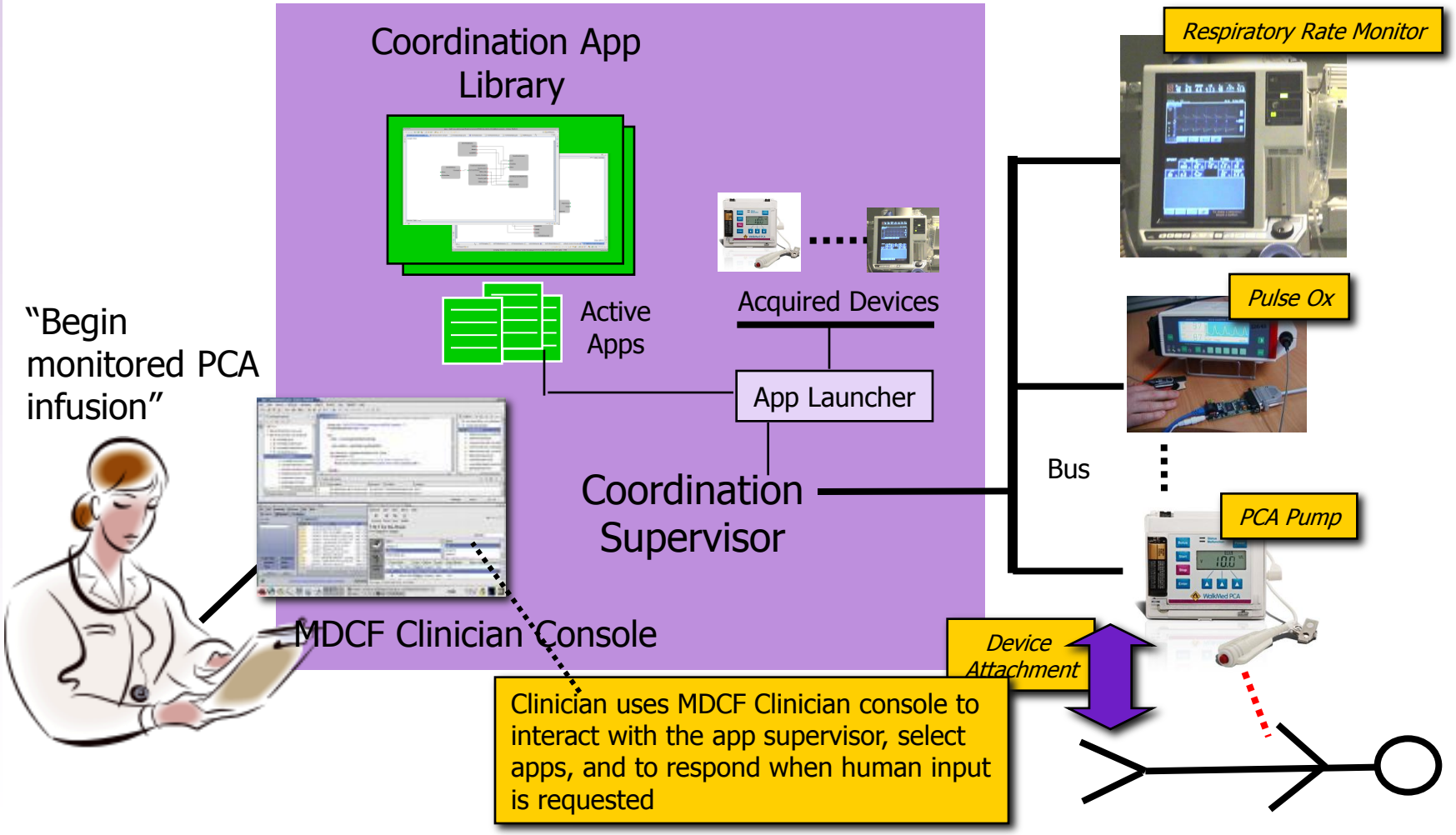


ICE Architecture (ASTM F2761-09)

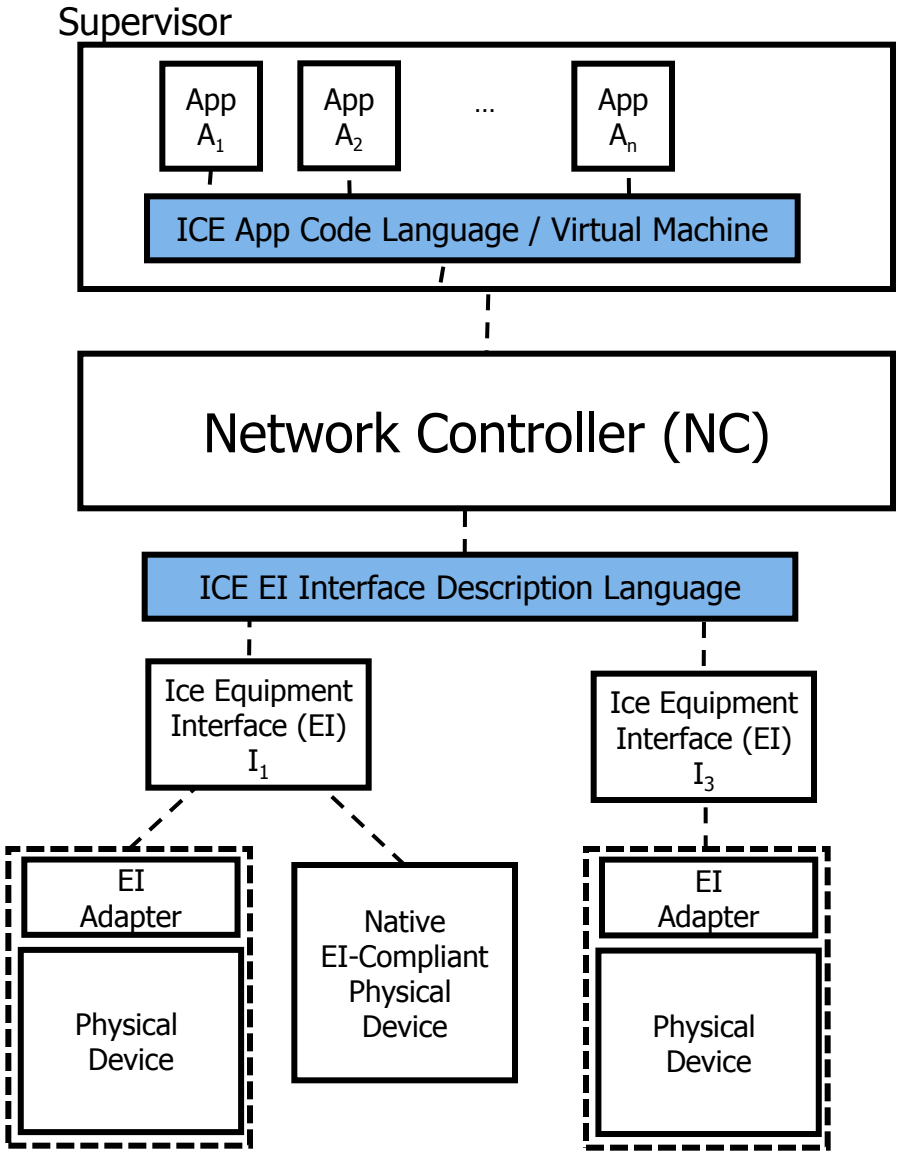
- Supervisor

  Virtual machine with separation kernel-like functionality that hosts apps that define the behavior of the system (clinical "intended use")

- Network Controller

  Middleware, MDDS + additional flexibility and real-time

- Compliant Devices
  - Native
  - Adapter-assisted



Opportunities

- Current regulatory policy does not allow integration platforms like the ones that I have described to be marketed
  - An opportunity to design/influence regulatory policy for such systems
- Envisioned "apps" are *virtual* medical devices; subjected to same regulations
  - More accessible to researchers in academia because they are *software-based* and *smaller in scale*
- Envisioned eco-system will rely on customized tool support
  - An opportunity to develop tools with the types of evidence-based techniques that we want to champion
- A number of dimensions (including both safety & security) are manifested within the framework
  - An opportunity to have a framework with the research community for addressing multiple dimensions

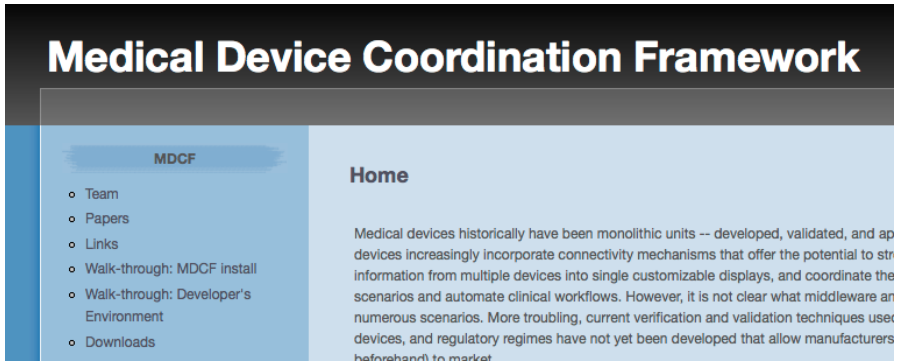
Funding

- NIBIB (NIH) Quantum – (PI -- Goldman, CIMIT) – 5 yr, $10million – Grouped with NSF SHARP Grants
- NSF CPS – (PIs, Hatcliff / Lee)

…both of these projects are tasked with producing open-source infrastructure, engaging in community building efforts, and providing science-based inputs to guide formation of regulatory policy.

Activities: Open Test Bed

We believe that these issues can only be addressed effectively by a broad community that includes academia, industry, and government regulatory agencies



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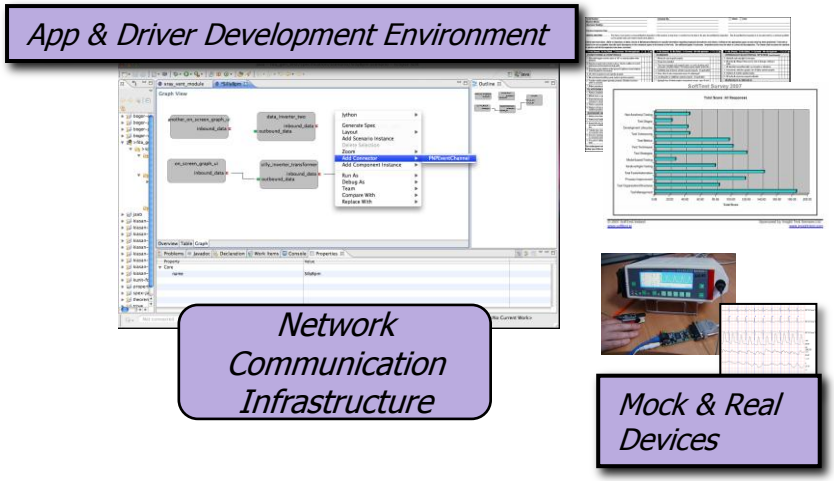
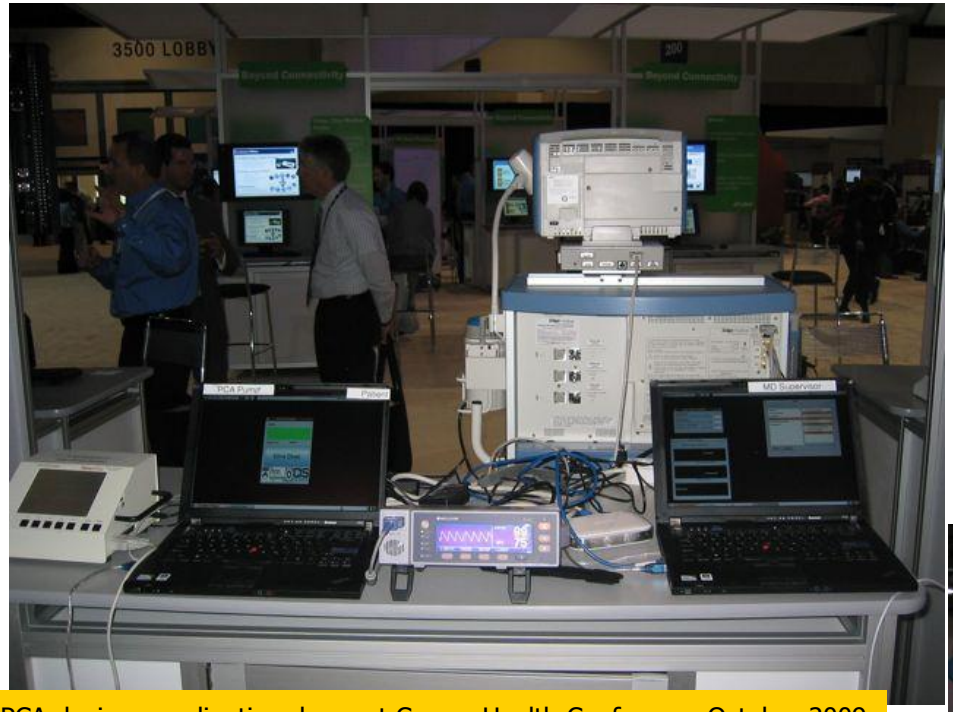


- Joint development between **KSU** and **U Penn** (NSF CPS funding)
- *Java-based open source* device coordination infrastructure built on **Java Messaging System** (e.g., *ActiveMQ* implementation)
- Simple infrastructure for building apps and interfacing with devices
- Mock (simulated) and real medical devices
- Being extended and enhanced by multiple research groups

MDCF Demo @ Cerner Health Conference



PCA device coordination demo at Cerner Health Conference October 2009

- 50-70 visitors with 10-15 in-depth conversations (15 minutes or longer)
- FDA representatives, Cerner engineers, device manufacturers, clinicians using Cerner products

Common responses

- "Oh, I had thought of that (*device coordination*). I can think of a lot of places where that would be useful."
  - One of the best examples was a solution for monitoring septic shock by the Technology Director of the University of Oklahoma Health Sciences Center
- "How are you going to get this by the FDA?"

U Penn Ph.D. student Andrew King explains demo scenario to Paul Jones from FDA

Challenge: Beyond "Pair-wise"

Current regulation of integrated systems (e.g., central station monitors) requires **"pair-wise" clearance**: whenever a new type of device is added to the monitoring platform, the entire infrastructure must be re-cleared.

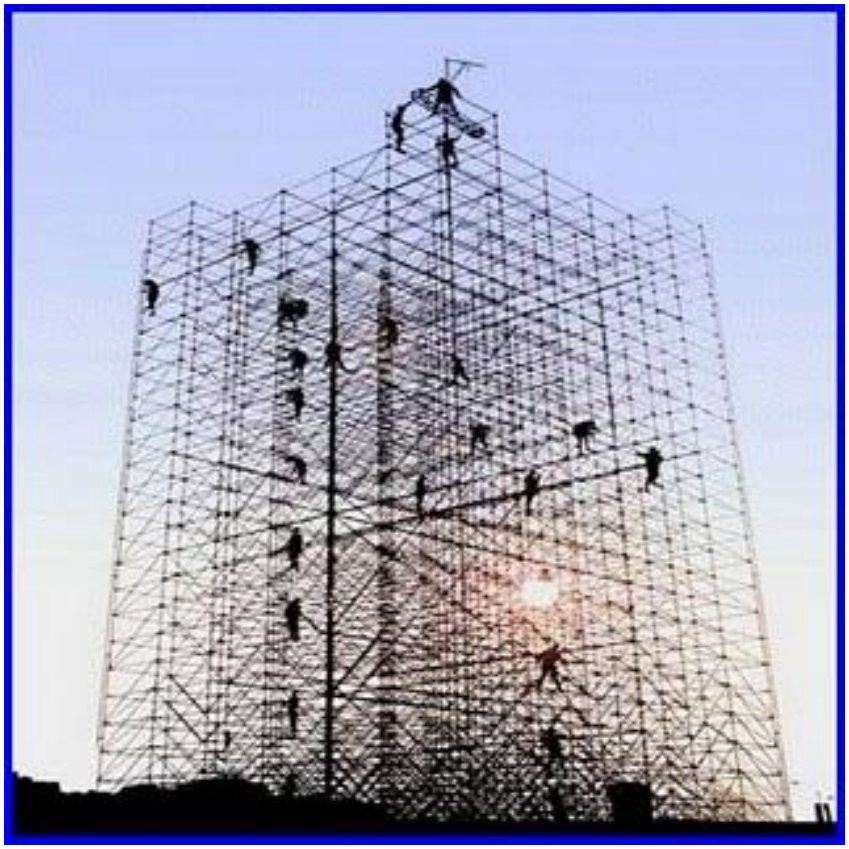
In "pair-wise" clearance, a monitoring station is "cleared" (and evaluated) against each of the device models that can be connected to it.

Following the existing "pair-wise" clearance approach will significantly limit the applicability of ICE and will inhibit the development of development of a commodity market of ICE components.

Challenge: need "compositional certification" – (a) how can the engineering challenges be addressed, (b) what is necessary to convince the FDA of the validity of the approach, and (c) how to communicate to the FDA the essential properties that must be in place for a compositional paradigm so that this does not establish a precedent for doing "bad things" in the future.

Challenge: Rigorous Regulatory Framework

- In contrast to other regulatory agencies, FDA is much more reluctant to mandate particular development approaches, specific artifacts, and verification techniques
- Existing submissions to FDA often vary widely in structure and in rigor
  - Harder to evaluate
  - Less amenable to tool support to aid/speed evaluation



Challenge: for this new paradigm of medical systems, how can we introduce a more rigorous regulatory structure that (a) **provides greater regularity/predictability** in the structure of submissions, (b) **emphasizes evidence-based arguments**, and (c) **enables greater tool support** for justification and evaluation of claims?

Challenge: Market Forces

- Well-designed **open platforms can encourage innovation** and give rise to an explosion in lightweight apps providing highly targeted functionality
- Likely be **many ICE apps and device interfaces submitted** for clearance – significantly more than the number of Class II & III device approvals that happen now
- **Safety in open systems is much more challenging**
  - **Apps need to maintain compatibility** with devices with which they have not been tested
  - Easier for "fly by night" operators to "roll their own" apps, interfaces, etc.

Challenge: existing regulatory process needs to be assessed with the goal of developing strategies for ICE-related submissions to better support **(a)** ***increased speed in processing submissions*****, and (b)** ***increased scrutiny of safety and functional/security claims***.

Current Trends

Example Trend: Cerner MDDS iAware App Store

CareAware iAware® Application Platform

"Organizations are able to purchase gadgets and perspectives from the Cerner Store as well as write and publish their own gadgets. The iAware platform supports the ability to plug these gadgets and perspectives into views to create a customized application based on the needs of a specific organization, role or venue."
– Cerner Marketing Material

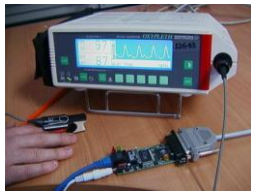
Note: iAware is an MDDS (data forwarding) platform, not a full device coordination (ICE-like) platform.

Activity: ICE Eco-sphere Roles

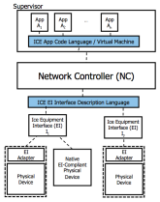
(excerpts)

Definition of roles, primary activities and processes associated with each role

Medical Device Manufacturer



ICE Equipment Originator



Augmented Device – paired with adapter to provide ICE interface

Health Care Delivery Organization

ICE Alliance

Organization of ICE Equipment Originators and other interested parties who cooperatively develop ICE standards, processes, and compliance evaluation procedures

ICE Alliance – Related Concepts

Similar relationships exist in other domains, e.g., FCC + WiFi, …

Regulatory Agency

- Recognizes standards and compliance certification of the alliance

Interoperability Standards Alliance

- Defines interoperability standards
- Develops compliance conformance tests
- Credentials third-party certifiers

ICE Entities: Primary Roles

ICE Alliance

Organization of ICE Equipment Originators and other interested parties who cooperatively develop ICE standards, processes, and compliance evaluation procedures

Architecture & Interfacing Standards

- Develop **interface/architecture standards for ICE components** such as the Network Controller, Supervisor, and Data Logger
- Develop and maintain a **standard for ICE Equipment (IE) Interface Definition Language (IDL)**
- Develop a **standard for clinical app programming language** that is used to specify the behavior of apps hosted by the Supervisor

ICE Entities: Primary Roles

ICE Alliance

Organization of ICE Equipment Originators and other interested parties who cooperatively develop ICE standards, processes, and compliance evaluation procedures

ICE Tools and Resources

- A well-organized **library of ICE Equipment interfaces**
- Test suites and **evidence-based tools for assessing ICE compliance** of proposed ICE components
- Templates and guidelines for consistently structured artifacts for clearance submissions to the Regulatory Authority

ICE Entities: Primary Roles

ICE Alliance

Organization of ICE Equipment Originators and other interested parties who cooperatively develop ICE standards, processes, and compliance evaluation procedures

Third-Party Testing/Evaluating Laboratories

- Organizations officially sanctioned by the ICE Alliance to test ICE submissions and judge compliance

ICE Entities: Primary Roles

Regulatory Authority

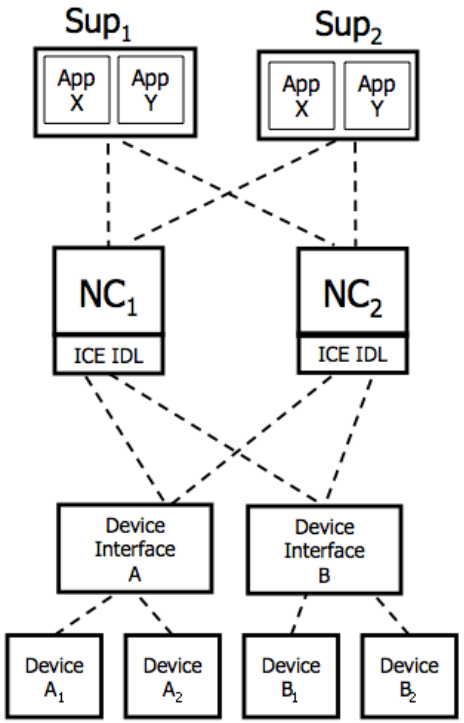
Issues clearance for devices and medical system components (such as ICE, ICE apps, etc.) with the goal of assuring safety and effectiveness for their intended use

For ICE…

- Recognize interface standards and process standards produced by the ICE Alliance
- **Process applications for "ICE clearance,"** i.e. submissions that claim that ICE Equipment (e.g. Network Controller, Supervisor, Supervisor app) **conforms to ICE standards** and is **safe and effective for use with ICE**
- Designate **third-party testing/evaluation labs**

Regulatory Demonstration

To communicate vision/concept to the FDA, a working group is putting together a collection of mock 510Ks (FDA regulatory submissions)



- Identify primary hazards, safety & effectiveness issues with each architecture component
- Interoperability compliance goals
- Illustrate processes throughout the ICE Ecosystem
- Collect requirements for tool support

Main Idea: Systematically switching between multiple versions of each component type to illustrate issues in composition certification/approval

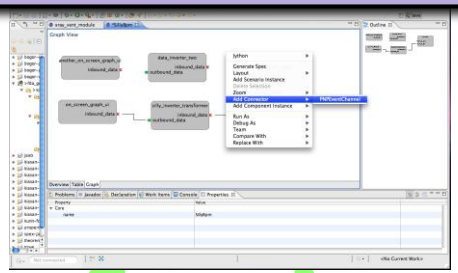
Tools

Take advantage of the domain-specific setting (dramatically limited scope) to provide a comprehensive environment for development, verification, certification, regulatory submissions

Development and Verification

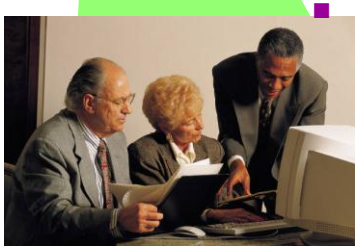
- Requirements templates
- Hazard analysis templates
- Safety control logic
- Interface specification and checking
- Compliance test suites
- Assurance case construction

App & Driver Development Environment



Developers

Evaluators



Regulatory Submission Construction

- Identify criticality level and conformance to common "patterns" of apps
- 510k templates, specialized to different ICE architecture component types
- Tracing to assurance case and evidence from development artifacts
- Automatically bundled for submission to third-party certifiers and regulatory authorities

Common Criteria Authoring Environment

The Common Criteria Authoring Environment (Delong & Rushby) may provide some inspiration for developing framework for constructing 510Ks and PMAs

CC Authoring Environment

- Addresses a setting that focuses on compositional construction
- Addresses a setting that aims to focus on developing a commodity market of components
- Provides a framework for defining *Protection Profiles* for different categories of components
- Common Threats/Policies for particular types of components
- Bundling of artifacts for review

ICE Authoring Environment

- Addresses a setting that focuses on compositional construction
- Addresses a setting that aims to focus on developing a commodity market of components
- Provides a framework for defining 510k template for different categories of components from the ICE architecture
- Common Hazards/Safety Goals for particular types of components and apps
- Bundling of artifacts for review

Note: ICE has several tie-ins to MILS architecture/philosophy

Summary – Technical Themes

- Recognizing the "cyber-physical systems" aspect of high-acuity health care, and putting infrastructure in place to monitor, control, and manage those systems
- Vision will require a radical departure from current FDA regulatory policy to allow a "compositional approach" to regulatory approval/certification
  - There is a strong tension between the two points above (we want to view as a system, but we certify component-wise)
  - The "key concept" here is that the assurance argument for the *app* which defines the *intended use* of the system states the claims related to system behavior and "imports" the assurance arguments from the infrastructure components
- A stringent third-party certification process uses shared tools to…
  - Mandate a regular structure to evidence-based certification submissions
  - Provides stringent compliance evaluation based on testing and formal techniques

Summary – Community Building

- Funded efforts on this project are mandated to produce resources for the broader community – SCC is ideal consumer (or even contributor)
- Technology and processes must be illustrated and evaluated to convince regulators
- Opportunities to contribute and evaluate…
  - Development technologies
  - Verification/Validation technologies
  - Development process design
  - Regulatory policy design
- Goal is to come back to next SCC meeting with an overview of a first collection of example artifacts
- Workshop/Tutorial at Automated Software Engineering conference, Nov. 11, 2011

Open Test Bed

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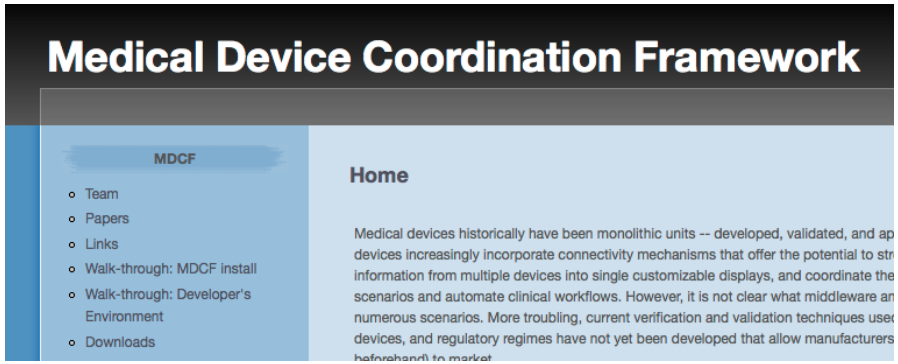

http://mdcf.santos.cis.ksu.edu

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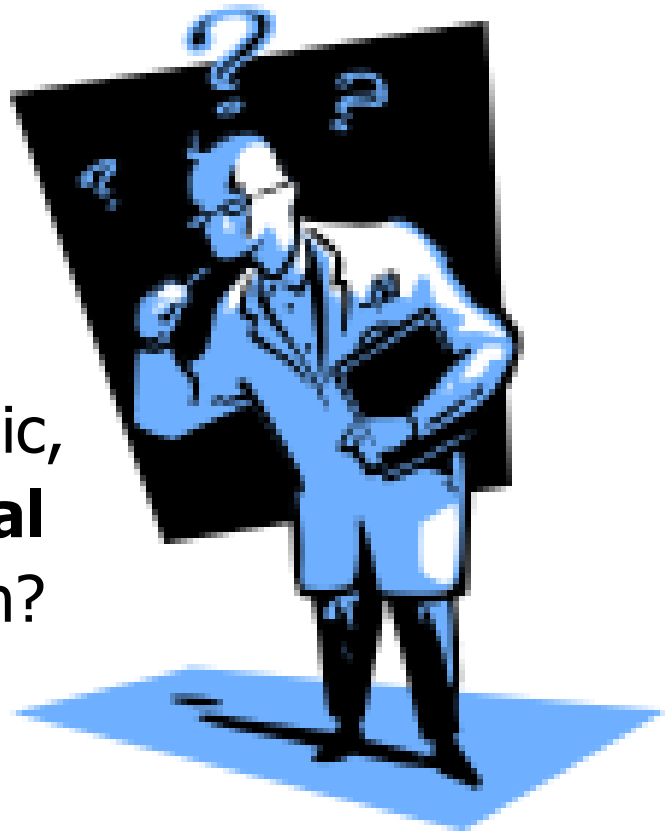
References

- John Hatcliff, Eugene Vasserman, Sandy Weininger, Julian Goldman, "An Overview of Regulatory and Trust Issues for the Integrated Clinical Environment", *High-Confidence Medical Device Systems and Software (HCMDSS 2011).*
- Andrew King, Sam Procter, Dan Andresen, John Hatcliff, Steve Warren, William Spees, Raoul Jetley, Paul Jones, Sandy Weininger. "An Open Test Bed for Medical Device Integration and Coordination"*, Proceedings of International Conference on Software Engineering (ICSE 2009), (Software Engineering in Practice Track).* ICSE-Companion, May 2009, pp. 141 - 151. IEEE Press.
- *Medical Device Plug-and-Play (MDPnP) Interoperability* web-site http://www.mdpnp.org
- *Medical Device Coordination Framework* web-site – http://mdcf.santos.cis.ksu.edu

Issues

- **Defining primary roles** in the ICE ecosphere
- **Identifying regulatory issues** with such systems
  - Market forces
  - Engineering considerations
- Verification, validation, and regulation
  - Which components may require regulatory clearance?
  - What are the key interoperability verification tasks?
- Point-of-care configurations are dynamic, so how can we **establish trust, in real time**, with minimal human intervention?



Medical Device Coordination Framework

Open experimental platform to bring together academic researchers, industry vendors, and government regulators

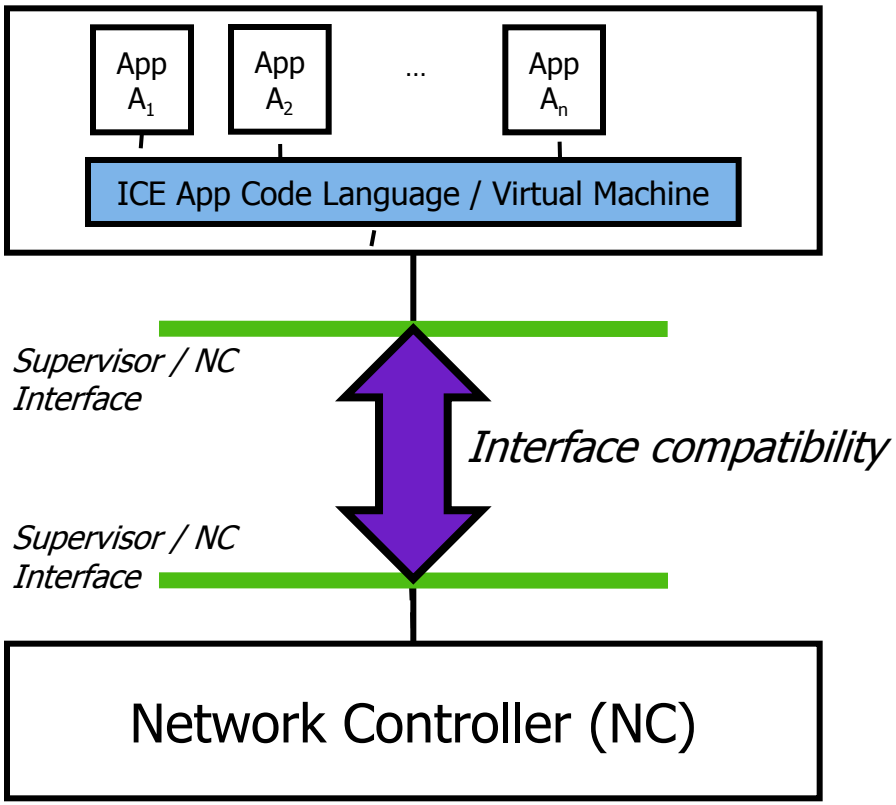
- Goals
  - Open source infrastructure
  - Meet performance requirements of realistic clinical scenarios
  - Provide an effective programming model and integrated development environment
  - Provide basic middleware-level reliability (e.g. guaranteed message delivery)
  - Modular and easy to extend with new devices, displays, health databases
  - Illustrate how to support real and mock devices

MD PnP Clinical Support

- Clinical societies endorsing device interoperability as envisioned in ICE
  - Anesthesia Patient Safety Foundation
  - Society of American Gastrointestinal Endoscopic Surgeons (SAGES)
  - World Federation of Anesthesiologists (WFSA)
  - Society for Technology in Anesthesia (STA)
  - American Society of Anesthesiologists (ASA)
  - Massachusetts Medical Society (MMS)

For ICE: "Component-wise"

The ICE vision emphasizes compositional or **"component-wise" clearance**: current regulatory authorities still need to be convinced that this approach can assure safety and effectiveness

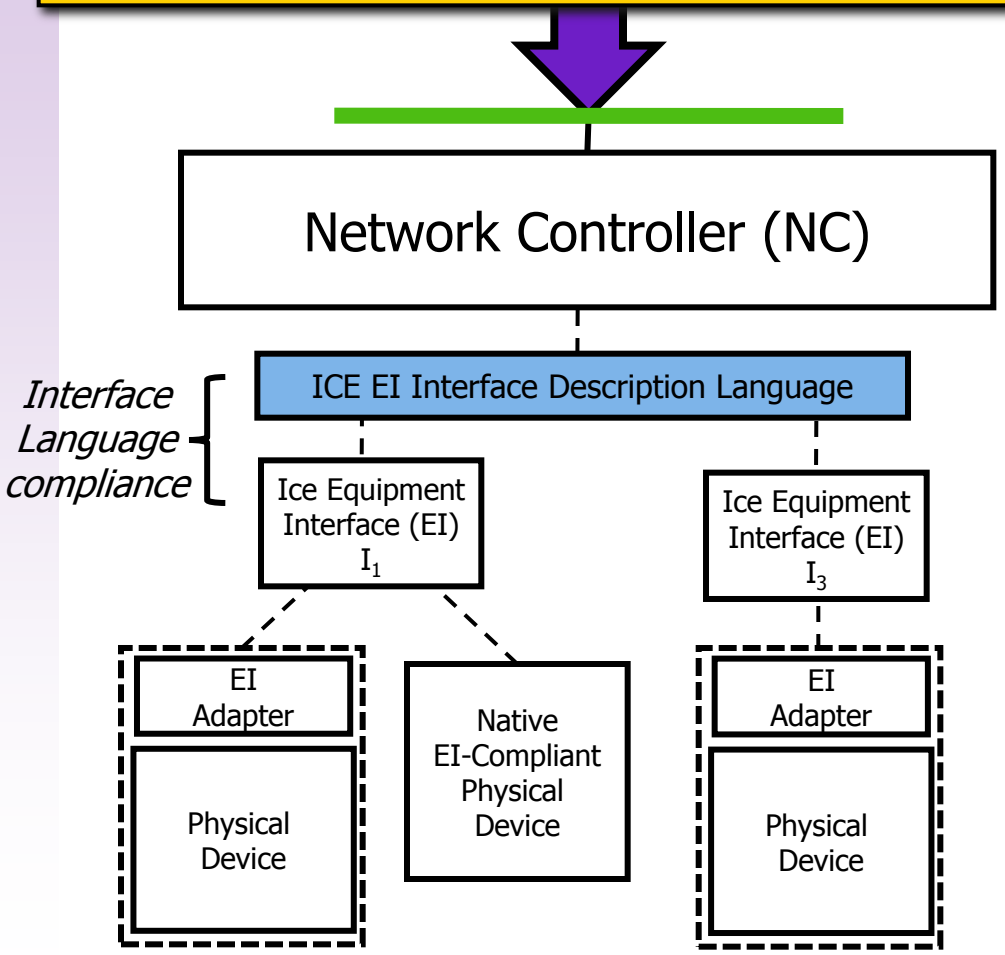


In ICE, standardized interfaces are defined between components, e.g. the Supervisor / Network Controller Interface

The Supervisor, instead of being cleared against a specific model of Network Controller (as required in the "pair-wise"), in component-wise clearance the Supervisor is cleared against the ICE standard Supervisor / NC interface

For ICE: "Component-wise"

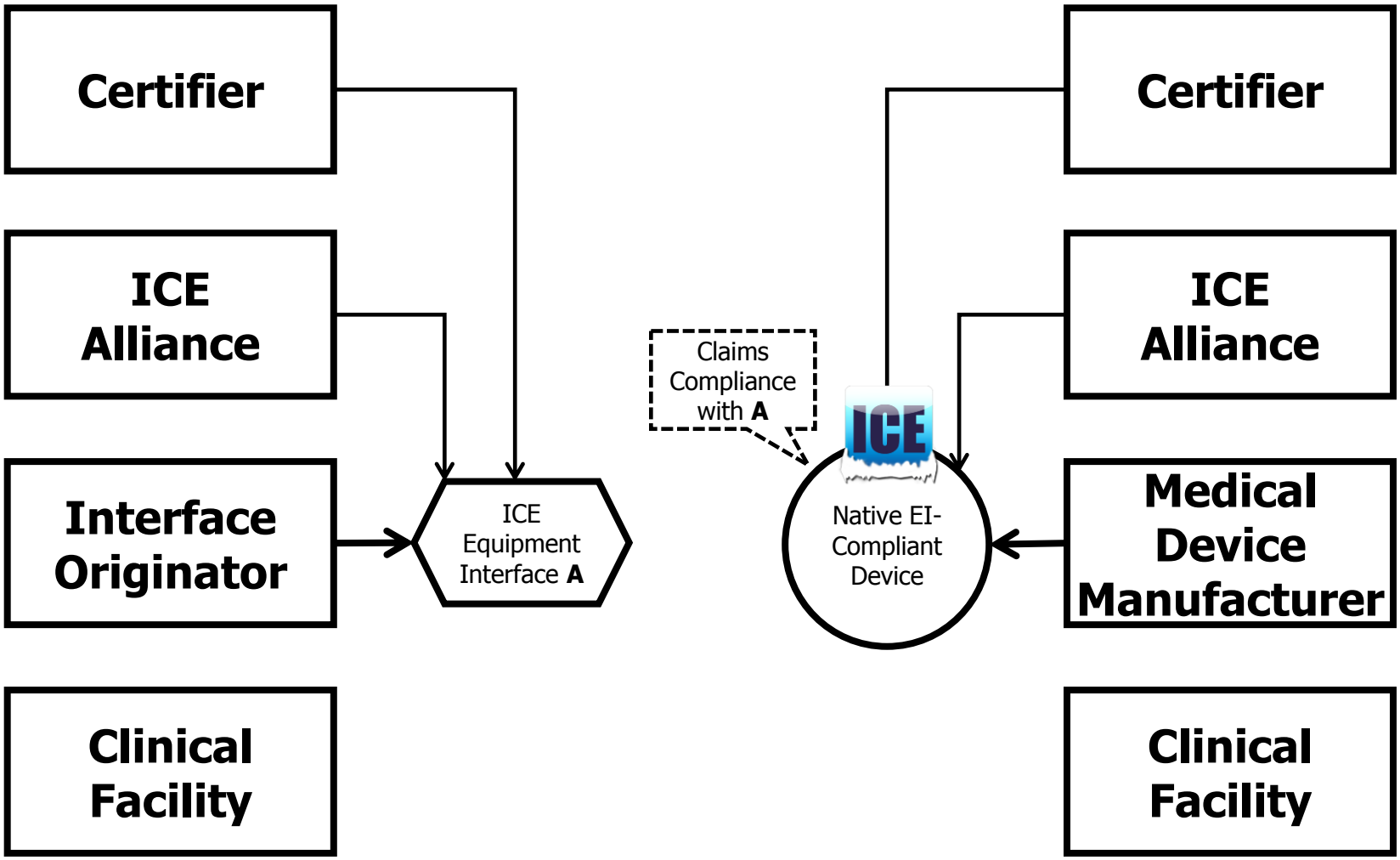
The ICE vision emphasizes compositional or **"component-wise" clearance**: current regulatory authorities still need to be convinced that this approach can assure safety and effectiveness



In ICE, all possible interfaces between NC and devices are cannot be known *a priori.* We need to support "variable interfaces" – interfacing between NC & devices that allows device interfaces to be different.

Variable interfacing will be achieved by defining an ICE Interface Description Language. A NC is cleared against the ICE IDL (showing that it can interface with any device whose interface is correctly describing using the IDL).

Trust Chains for ICE Components



Validation and Certification